Poly((4-dihydroxyborophenyl)acetylene) as a Novel Probe for Chirality and Structural Assignments of Various Kinds of Molecules Including Carbohydrates and Steroids by Circular Dichroism

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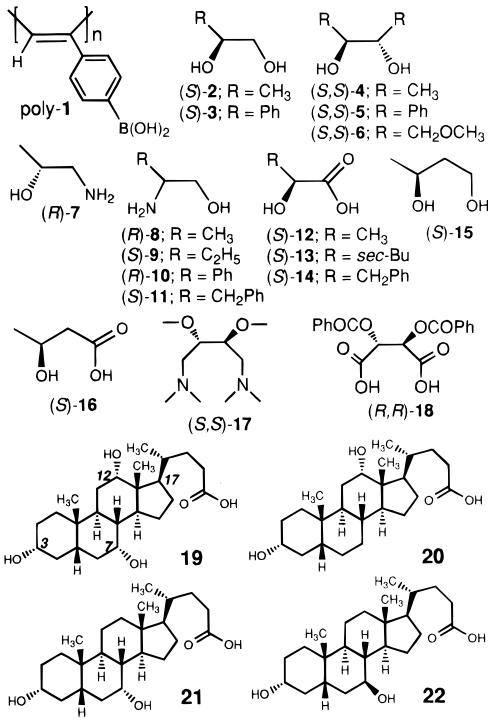
Boronic acids are known to form a complex with diol-containing compounds including carbohydrates, and boronates immobilized in polymer matrices have been exploited in affinity chromatography[1] for the separation of tRNA, glycoproteins, and carbohydrates enantiomers.[2] Aromatic boronic acids have been used as synthetic carriers of carbohydrates and ribonucleosides for selective membrane transport,[3] chemosensors[4] and receptors[5] of mono- and disaccharides, and chiral resolving agents of diols and diamines in NMR.[6] In these studies, covalent complex formation between the aromatic boronic acids and diols or carbohydrates was the key for molecular recognition.[1−6] However, limited studies have dealt with the complex formation of aromatic boronic acids with other difunctional chiral molecules such as amino alcohols, hydroxycarboxylic acids, dicarboxylic acids, diamines, and amino acids.[7]

Recently, we have found that an achiral, stereoregular poly-((4-carboxyphenyl)acetylene) can change its structure into a prevailing one-handed helix upon complexation with chiral amines, and its helical sense can be used as a probe for the chirality assignment of amines using the circular dichroism (CD) of the complexes.[8] However, the polymer is not sensitive to other important chiral molecules in organic and natural products chemistry (for instance, diols, polyols, and carboxylic acids). Here, we report the complex formation of various kinds of acyclic and cyclic chiral molecules with two or more functional groups (Chart 1) including carbohydrates and steroids with a novel stereoregular poly(phenylacetylene) derivative, poly((4-dihydroxyborophenyl)acetylene) (poly-**1**),[9] which induced a prevailing helical conformation accompanied by a split-type induced CD (ICD). Although the CD exciton chirality method developed by Nakanishi and Harada[11] has been extensively applied for determining the absolute configurations of chiral molecules, the method requires the introduction of chromophores suitable for the exciton coupling at hydroxy or amino groups.[12] The present ICD method using poly-**1** requires no derivatization, may be applicable for the chirality assignment of a broad range of chiral molecules including carbohydrates and steroids, and can be used as a suitable tool for evaluating the interaction between aromatic boronic acids and chiral molecules bearing

Chart 1. Structures of Poly-**1** and **2**−**22**



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(9) Poly-**1** was obtained by polymerization of (2,2-dimethylpropane-1,3-diyl)[*p*-(ethynyl)phenyl]boronate with $[Rh(nbd)Cl]_2$ (nbd: norbornadiene), followed by hydrolysis of the protecting group. The ^1H NMR spectra of poly-**1** in D_2O-CD_3OD (9/1) and the original polymer in $CDCl_3$ showed a sharp singlet centered at 5.93 and 5.78 ppm, respectively, due to the main chain protons, indicating that these polymers possess a highly cis-transoidal, stereoregular structure.[10]

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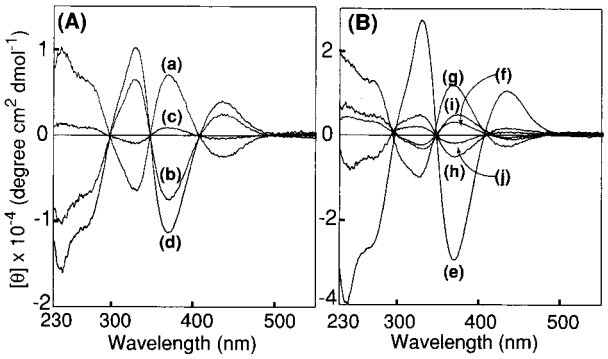

Figure 1. CD spectra of poly-**1** with (A) (*S*,*S*)-**4** (a), (*R*,*R*)-**4** (b), (*S*)-**2** (c), and (*S*)-**15** (d) and (B) (*R*)-**7** (e), (*R*)-**8** (f), (*S*)-**12** (g), (*S*)-**16** (h), (*S*,*S*)-**17** (i), and (*R*,*R*)-**18** (j); molar ratio to monomeric units of poly-**1** is 5 (a−f), 20 (j), and 50 (g−i). The CD spectra were measured on a Jasco J-720 L spectropolarimeter in H_2O−methanol (9/1) (a−f) and (1/1) (g−j) at pH 11.6 (a−f), 6.3 (g and h), 10.6 (i), and 2.5 (j) in a 0.05 cm quartz cell at ambient temperature (*ca.* 20−22 °C) with a poly-**1** concentration of 1.0 mg/mL.

two or more functional groups, which has not been fully understood so far.

Figure 1A shows typical CD spectra of poly-**1** in the presence of the chiral 1,2- and 1,3-diols (*S*)-**2**, (*S*,*S*)- and (*R*,*R*)-**4**, and (*S*)-**15** in H_2O−methanol (9/1) at pH 11.6. The complexes showed characteristic, split-type ICDs, and the enantiomers of **4** gave ICDs which are mirror images.[13] Poly-**1** formed complexes with other chiral molecules such as 1,2-amino alcohols (**7**−**11**), 1,1- and 1,2-hydroxycarboxylic acids (**12**−**14** and **16**), a 1,4-diamine (**17**), and a 1,2-dicarboxylic acid (**18**) (Figure 1B) that show ICDs similar to Figure 1A.[14] These ICD results indicate that these chiral molecules can sufficiently interact with the boronic acid residues of poly-**1** to induce the helical conformation with a predominant screw sense,[8] probably by tetragonal (sp^3 hybridization) complex formation with the chiral molecules in solution.[1,2,5,15]

The split-type and magnitude of the Cotton effects seem to be closely correlated with the stereochemistry and configuration of the molecules. All 1,2-diols (**2**−**6**) and 1,1-hydroxycarboxylic acids (**12**−**14**) tested in this study, 1-amino-2-propanol (**7**), **17**, and **18** gave the same Cotton effect signs depending on the configuration. However, 2-amino 1-alcohol derivatives (**8**−**11**), 1,3-diol (**15**), and 1,2-hydroxycarboxylic acid (**16**) showed the opposite sign compared with other 1,2-difunctional compounds.[16]

*It is worth noting that poly-**1** showed ICDs in the presence of steroids with remote stereogenic centers*, although the magnitude of the ICDs was weak. The complexes with **19** and **21** having an α-OH group at the 3 and 7 positions showed the same ICD signs, while the complexes with **20** and **22** with no α- or β-OH group at the 7 position showed the opposite sign or almost no ICD at pH 5, respectively (see supporting information). These results suggest that the multiple interaction between the remote α-hydroxy and/or carboxy groups of the steroids and a sequence of boronic acid residues of poly-**1** may be responsible for the complex formation and the ICD.

As expected, poly-**1** can form a complex with mono- and disaccharides, and these complexes exhibit a characteristic ICD. Preliminary CD experiments were carried out using D- and L-glucose, D-mannose, D-galactose, D-arabinose, D-ribose (monosaccharides), D-cellobiose, D-maltose, D-lactose, and D-sucrose (disaccharides). The split-type and magnitude of the Cotton effects appear to reflect the stereochemistry and configuration of the carbohydrates. Glucose gave the most intense ICD ($[\theta]_{364}$ +21600; [D-glucose]/[poly-**1**] = 5 at pH 11.6), while L-glucose, D-arabinose, and D-sucrose showed the opposite ICD signs compared with the other D-carbohydrates (see supporting information).

In summary, poly-**1** provides a new promising probe for chirality assignments and stereochemical studies of various kinds of chiral molecules including carbohydrates and steroids and will be applicable as a sensory system of chiral molecules including biopolymers such as polysaccharides, glycoproteins, and RNA and also for the solid membrane transport system.

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Supporting Information Available: Experimental procedures, computational calculations, ^{13}C NMR data of the model complexes, spectroscopic data of poly-**1**, and figures of UV spectrum of poly-**1** and CD spectra of the complexes of poly-**1** with **19**, **20**, and carbohydrates (8 pages). See any current masthead page for ordering and Internet access instructions.

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(13) There are at least four Cotton effects with the exciton-type splittings in the ICDs. However, the assignments of the Cotton effects have not yet been done. The complexes with the other chiral 1,2-diols (*S*)-**3**, (*S*,*S*)-**5**, and (*S*,*S*)-**6** showed similar ICDs with the same Cotton effect signs depending on the configuration; molar ellipticities ($[\theta] \times 10^{-3}$ (degree cm^2 dmol^{-1}) and λ (nm)) of the second Cotton for the complexes were 3.8 (372), 14 (379), and 1.3 (365), respectively.

(14) Molar ellipticities ($[\theta] \times 10^{-3}$ (degree cm^2 dmol^{-1}) and λ (nm)) of the second Cotton for the complexes with (*S*)-**9**, (*R*)-**10**, (*S*)-**11**, (*S*)-**13**, and (*S*)-**14** were −9.4 (370), 5.6 (374), −15 (372), 17 (368), and 18 (371), respectively.

(15) The magnitude of the ICDs was significantly influenced by pH. The influence of the pH on the ICD was investigated for the mixtures of poly-**1** with (*S*,*S*)-**4**, (*R*)-**7**, (*S*)-**12**, or (*S*)-**16** (see supporting information).

(16) For detailed discussion on the basis of the semiemperical molecular orbital calculations (MOPAC, AM1) and ^{13}C NMR studies of the model complexes with respect to the relation between the split-type of the Cotton effects and configuration of the molecules, see the supporting information.